

Human Papillomaviruses and Cancer

Human Papillomaviruses

Human papillomaviruses (HPVs) are a group of more than 80 types of viruses. They are called papillomaviruses because certain types may cause warts, or papillomas, which are benign (noncancerous) tumors. Different types of HPVs cause the common warts that grow on hands and feet and those that develop in the mouth and genital area.

Of the more than 80 types of HPVs, there are more than 30 types that have the ability to infect the genital tract. These genital HPVs can be passed from one person to another through sexual intercourse. Some HPVs may cause warts to appear on or around the genitals and anus of both men and women. Genital warts are known technically as condylomata acuminatum and are generally associated with two HPV types, numbers 6 and 11. HPVs may also cause flat, abnormal growths in the genital area and the cervix (the lower part of the uterus which extends into the vagina).

HPVs and Cancer Risk

HPVs are now recognized as the major cause of cervical cancer. Some types of HPVs are referred to as “low-risk” viruses because they rarely develop into cancer; these include HPV-6 and HPV-11. HPV viruses that can lead to the development of cancer are referred to as

“cancer-associated types.” Sexually-transmitted, cancer-associated HPVs have been linked with cancer in both men and women; most importantly they include HPV-16, HPV-18, HPV-31, and HPV-45. These cancer-associated types of HPVs cause growths that usually appear flat and are nearly invisible, as compared with the warts caused by HPV-6 and HPV-11.

Precancerous Conditions

Both cancer-associated types and low-risk types of HPVs can cause the growth of abnormal cells in the cervix, but generally only the cancer-associated types of HPVs may lead to cervical cancer. Abnormal cervical cells can be detected when a Pap test is done during a gynecologic exam. Several different terms have been used to describe the abnormal cells that may be seen in Pap tests. In the Bethesda system (the major system used to report the results of Pap tests in the United States), precancerous conditions are divided into low-grade and high-grade squamous intraepithelial lesions (SILs). Squamous cells are thin, flat cells found in the tissue that forms the surface of the skin, the lining of the upper passages of the respiratory and digestive tracts, and the vagina and outer cervix. Other terms sometimes used to describe these abnormal cells are cervical intraepithelial neoplasia (CIN) and dysplasia. Low-grade SILs (mild dysplasias) are a common condition, especially in young women. The majority of low-grade SILs return to normal over months to a few years. Sometimes, low-grade SILs can progress to high-grade SILs. High-grade SILs are not cancer, but they may eventually lead to cancer and should be treated by a doctor.

Behaviors such as beginning sexual intercourse at an early age and having many sexual partners increase the chance of getting an HPV infection. Most infections with HPV go away on their own without causing any type of abnormality. It is important to note that infection with

cancer-associated HPV types (16, 18, 31, and 45) may increase the risk that mild abnormalities will progress to more severe abnormalities or cervical cancer. Still, of the women who do develop abnormal cell changes with cancer-associated types of HPV, only a small percentage would develop cervical cancer if these cells were not removed. Studies suggest that whether a woman will develop cancer depends on a variety of factors acting together with cancer-associated HPVs. These factors may include smoking, decreased resistance to infection, and infection with agents other than HPVs.

Followup and Treatment

If worrisome cell changes are found on a Pap test, the next step is usually colposcopy and biopsy of any abnormal areas. (Colposcopy is a procedure in which a lighted magnifying instrument called a colposcope is used to examine the vagina and cervix. Biopsy is the removal of a small piece of tissue for diagnosis.)

Although there is currently no medical cure to eliminate a papillomavirus infection, the SILs and warts these viruses cause can be treated. Methods used to treat SILs include cold cautery (freezing that destroys tissue), laser treatment (surgery with a high-intensity light), LEEP (loop electrosurgical excision procedure, the removal of tissue using a hot wire loop), as well as conventional surgery. Similar treatments may be used for external genital warts. In addition, two powerful chemicals (podophyllin and trichloroacetic acid) will destroy external genital warts when applied directly to them. Imiquimod cream has also been recently approved by the Food and Drug Administration (FDA) as an effective drug treatment. Imiquimod works by stimulating the immune system to fight the virus.

Current Research

A major study at the National Cancer Institute (NCI) is currently evaluating different management approaches for women with mildly abnormal Pap test results. The findings will help women and their doctors decide what course of action to take when mild abnormalities show up on Pap tests. NCI researchers are also testing and validating new ways to screen for HPV and related cervical cell changes.

NCI laboratory scientists are conducting research on HPVs to learn how they cause precancerous changes in normal cells as well as how to prevent these changes. They are studying HPVs grown in the laboratory with the goal of finding ways of controlling the infection or making a vaccine against the viruses. Scientists have developed several promising vaccines for related papillomaviruses that are currently being tested in animals. In addition, they are attempting to learn how to help a person's own immune (defense) system to prevent the progression of abnormal cervical cells to cervical cancer.

Laboratory research results indicate that HPVs produce proteins known as E5, E6, and E7. These proteins interfere with the cell functions that normally prevent excessive growth. For example, HPV E6 interferes with the human protein p53. p53 is present in all people and acts to keep tumors from growing. This research may be useful in developing ways to interrupt the process by which HPV infection may lead to growth of abnormal cells and eventually cancer.

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Sources of National Cancer Institute Information

Cancer Information Service

Toll-free: 1-800-4-CANCER (1-800-422-6237)

TTY (for deaf and hard of hearing callers): 1-800-332-8615

NCI Online***Internet***

Use <http://www.cancer.gov> to reach NCI's Web site.

CancerMail Service

To obtain a contents list, send e-mail to cancermail@icicc.nci.nih.gov with the word "help" in the body of the message.

CancerFax® fax on demand service

Dial 301-402-5874 and listen to recorded instructions.

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